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09/744,146	03/29/2001	Masayuki Machida	10287.39	3956

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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,146	MACHIDA ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-11 and 35-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11 and 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 8-11 and 35-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

3. For convenience, claims 35-37, the only independent claims under consideration on the merits, are reproduced below.

35. (Currently Amended) A labeled complex, comprising:

a carrier particle selected from the group consisting of a magnetic particle, charged particle, dielectric, chemotactic microorganism, synthetic resin bead, latex particle, glass bead, gel substance, and a metallic particle;

a number of target receptors of length up to 10 microns, each receptor having a first end and a second end, wherein the first end of each receptor is bonded with said carrier particle,

wherein said target receptors are single-stranded nucleic acids ~~of predetermined base sequence~~, wherein the single-stranded nucleic acid is ~~a base sequence of~~ a gene, ~~a base sequence of~~ mRNA, ~~a base sequence of~~ tRNA, ~~a base sequence of~~ rRNA, ~~a base sequence~~ a single-stranded nucleic acid obtained by denaturation of a double stranded nucleic acid or ~~a base sequence~~ obtained by synthesis~~, and~~

~~wherein said target receptors bonded with a single carrier particle have the same or different base sequences~~;

and

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the second end of each receptor, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances, in all of said labeled substances of the carrier particle;

wherein the number and length of target receptors bonded to said carrier particle is such that ~~a major influence by~~ energy movement among the labeled substances and ~~or~~ occurrence of quenching are prevented ~~among the labeled substances does not occur,~~ thereby enhancing consistent discrimination of ~~by stable~~ emissions.

36. (Currently Amended) A labeled complex, comprising:

a carrier particle selected from the group consisting of a magnetic particle, charged particle, dielectric, chemotactic microorganism, synthetic resin bead, latex particle, glass bead, gel substance, and a metallic particle;

a number of target receptors of length up to 10 microns, wherein said target receptors are double stranded nucleic acids ~~of predetermined base sequence~~, each double stranded nucleic acid having a first single strand and a second single strand, each single strand having a first and a second end, wherein the target receptor has a first end of a first single strand bonded with said carrier~~, and wherein said target receptors bonded with a single carrier particle have the same or different base sequences~~, wherein the double-stranded nucleic acid is ~~a base sequence of~~ a gene, ~~a base sequence of mRNA, a base sequence of tRNA, a base sequence of rRNA, a base sequence~~ a double stranded nucleic acid obtained by using the polymerase chain reaction, ~~a base sequence~~ a double stranded nucleic acid having a recognition sequence of a restriction enzyme at one end, a ~~base sequence~~ double stranded nucleic acid generated by annealing, or a double stranded nucleic acid ~~base sequence~~ generated by DNA ligase;
and

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the second end of a second single strand, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances, in all of said labeled substances of the carrier particle;

wherein the number and length of target receptors bonded to said carrier particle is such that ~~a major influence by~~ energy movement among the labeled substances and ~~or~~ occurrence of quenching are prevented ~~among the labeled substances does not occur,~~ thereby enhancing consistent discrimination of ~~by stable~~ emissions.

37. (Currently Amended) A labeled complex, comprising:

a carrier particle selected from the group consisting of a magnetic particle, charged particle, dielectric, chemotactic microorganism, synthetic resin bead, latex particle, glass bead, gel substance, and a metallic particle;

a number of target receptors of length up to 10 microns, wherein said target receptors are double stranded nucleic acids ~~having a predetermined base sequence~~, each double stranded nucleic acid having a first single strand and a second single strand, each single strand having a first and a second end, wherein the target receptor has a second end of a first single strand bonded with said carrier; ~~wherein said target receptors bonded with a single carrier particle have the same or different base sequences~~; wherein the double-stranded nucleic acid is ~~a base sequence of~~ a gene, ~~a base sequence of mRNA, a base sequence of tRNA, a base sequence of rRNA, a base sequence~~ a double-stranded nucleic acid obtained by using the polymerase chain reaction, a double-stranded nucleic acid ~~a base sequence~~ having a recognition sequence of a restriction enzyme at one end, a double-stranded nucleic acid ~~a base sequence~~ generated by annealing, or a double-stranded nucleic acid ~~a base sequence~~ generated by DNA ligase;
and

at least a first type and a second type of labeled substance, each labeled substance bonded to a fraction of the number of target receptors at the first end of a first single strand, thereby forming a labeled complex having a predetermined molar ratio of the types of labeled substances in all of said labeled substances of the carrier particle;

wherein the number and length of target receptors bonded to said carrier particle is such that ~~a major influence by~~ energy movement among the labeled substances and ~~or~~ occurrence of quenching are prevented ~~among the labeled substances does not occur,~~ thereby enhancing consistent discrimination of ~~by stable~~ emissions.

4. For purposes of examination, claims 8-11 and 35-37 are construed as being drawn to products and not to a method of making same. Further, said claims, in the context of claim 35-37, and claims 8-11 that depend therefrom, have been construed as encompassing any gene, be it complete or partial, from any and all manner of life forms. Said claims have also been construed as encompassing virtually any nucleic acid.

5. Claim 35, while stating that the "target receptor" is a single stranded nucleic acid "bonded with [a] carrier particle," has been construed as encompassing nucleic acid that is bonded either directly or indirectly with said carrier particle. In the case of indirect bondedness, such limitation has been further construed as encompassing both partial and fully double

stranded and/or triplex nucleic acid structures. Claims 35 and 8-11 that depend therefrom have also been interpreted as encompassing any and all manner of rRNA, tRNA, and mRNA. While the claims have been amended so to remove the limitation that the nucleotide sequence is "predetermined," said claims have been construed as encompassing this very limitation, as well as encompassing nucleic acids for which the nucleotide sequence is unknown.

6. Claims 36 and 37 have been construed as encompassing any double stranded nucleic acid, be it generated by polymerase chain reaction or by some other means. While the claims recite that the nucleic acid is to be the product of a polymerase chain reaction, the claims are drawn to a product and not a process. With the claims fairly encompassing virtually any method of producing nucleic acids, the claims, in turn, have been construed as encompassing any and all possible nucleic acids that can be produced by such methods, regardless of whether the nucleic acid was actually produced by such means.

7. The complex of claims 35-37 has also been interpreted as requiring at least two labeling substances bound to different fractions of any number of target receptors and that the labeled complex has a "predetermined molar ration of the types of labeled substances."

8. US Patent 6,465,241 B2 (Haronian et al.), column 14, second full paragraph, teach that the length of axial rise per nucleotide in DNA is 3.3 Angstroms or 3.3×10^{-4} micrometers. In view of this teaching, applicant's single stranded nucleic acid would be 30,303 nucleotides long. Accordingly, applicants nucleic acid of a predetermined base sequence, be it a gene, tRNA, rRNA, mRNA, PCR product, comprising a restriction site at one end, is the product of annealing or of synthesis, would have a length up to 30,303 bases.

9. A review of the disclosure fails to find an adequate written description of any one embodiment where a nucleic acid has a length of 30,303 bases, be said nucleic acid tRNA, mRNA, rRNA, a gene, etc.

10. A review of the disclosure fails to find where any Sequence Listing of any nucleic acid has been provided. Yet, as seen in independent claims 35-37, the claims are drawn to a complex that is required to comprise nucleic acids of a predetermined sequence.

11. The failure of the disclosure to set forth any nucleic acids labeled with different labels in a "predetermined molar ratio," even when the nucleic acids have the same length and differ by but a single nucleotide does not reasonably suggest that applicant had possession of such a complex. Further, the absence of a description of such mandatory components fails to satisfy the written description requirement of 35 USC 112, first paragraph. It appears that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness. Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966:

> Recently, we held that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention.

For the above reasons, and in the absence of convincing g evidence to the contrary, claims 8-11 and 35-37 are rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement.

Response to argument

12. At page 6 of the response of 20 October 2004, hereinafter the response, applicant's representative asserts:

> In the presently claimed invention, no specific sequence is required or claimed. All nucleic acids have the structure-function relationship known to those of ordinary skill in the art for use in the present invention.

13. The above argument has been fully considered and has not been found persuasive. It is noted that applicant has defined the claimed nucleic acids as being either genes, tRNA, rRNA, mRNA, etc. These nucleic acids, while all being a "nucleic acid," do not share the same structure function relationship. Such labels go to identify how the various nucleic acids are to function, not describe what they are. The specification does not provide an adequate written description so to distinguish one tRNA, mRNA, DNA, etc., from another. Further, with the specification not providing a single Sequence Listing, or identify a single nucleic acid in terms of what it encodes, etc., does not reasonably suggest that applicant, at the time of filing, was in possession of the claimed genus of compounds claimed. Attention is directed to the decision of *Fiers v. Sugano* 25 USPQ2d 1604-5 (CAFC, January 1993) wherein is stated:

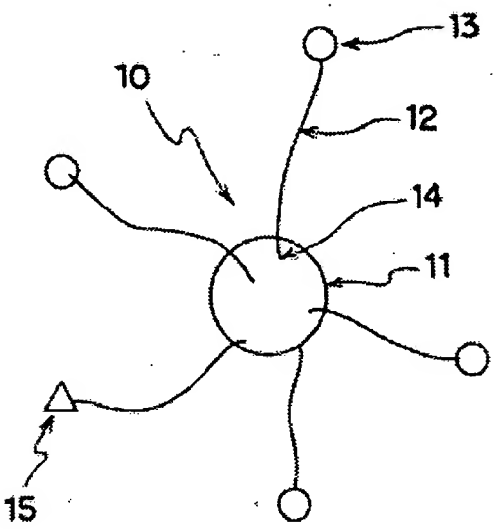
> We also reject *Fiers* argument that the existence of a workable method for preparing a DNA establishes conception of that material. Our statement in *Amgen* that conception may occur, *inter alia*, when one is able to define a chemical by its method of preparation requires that the DNA be claimed by its method of preparation. We recognize that, in addition to being claimable by structure or physical properties, a chemical material can be claimed by means of a process. A product-by-process claim normally is an after-the-fact definition, used after one has obtained a material by a particular process. Before reduction to practice, conception only of a process for making a substance, without a conception of a structural or equivalent definition of that substance, can at most constitute conception of the substance claimed as a process. Conception of a substance claimed *per se* without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties. . .
> * * * *

> The difficulty that would arise if we were to hold that a conception occurs when one has only an idea of a compound, defining it by its hoped-for function, is that would-be inventors would file patent applications before they had made their inventions and before they could describe them. That is not consistent with the statute or the policy behind the statute, which is to promote disclosure of inventions.

Attention is also directed to the decision of *University of California v. Eli Lilly and Co.* (CA FC, July 1997) 43 USPQ2d 1398 wherein is stated:

> In claims involving chemical materials, generic formulas usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate written description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what it achieves as a result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. *See In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.
>
> Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA. See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

While agreement is reached with applicant in that the specification does provide literal support for the use of the various terms, the mere presence of such phraseology, even when coupled with figures, e.g., Fig. 1A, below,



does not rise to the level of an adequate written description of the nucleic acids claimed.

14. At page 6 of the response argument is advanced that the specification sets forth lengths of the claimed nucleic acids.

15. This argument ahs been fully considered and has not been found persuasive as limitations found within the body of the disclosure are not read into the claims.

16. At page 6, bridging to page 7 of the response, argument is advanced that the claims recite that the nucleic acid is the product of polymerase chain reaction.

17. In response to the above argument, attention is directed to MPEP 2113 [R-1], reproduced in part below.

2113 [R-1] Product-by-Process Claims

PRODUCT-BY-PROCESS CLAIMS ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does

not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (Citations omitted)

18. In response to argument advanced at page 6 of the response that if the patent issued to O'Neil et al., encompasses the claimed invention, then the present disclosure must also satisfy the written description requirement, it is noted that each application for patent is considered on a case-by-case basis. It is further noted that unlike the present application, the disclosure of O'Neil et al., does in fact comprise a sequence listing.

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claims 8-11 and 35-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

21. Claims 8-11 and 35-37 are confusing as a result of the following phrase newly added to each of claims 35-37: "in all of said labeled substances of the carrier." The second usage of the word "of" may be at the core of the issue of indefiniteness.

Claim Rejections - 35 USC § 102/103

22. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

23. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

25. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

26. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

27. Claims 8-11 and 35-37 are rejected under 35 U.S.C. 102(a and e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 6,124,092 (O'Neil et al.).

28. As noted above, claims 8-11 and 35 have been interpreted as encompassing both direct and indirect bonding of the single stranded nucleic acid to the carrier particle. In the context of indirect bonding, the single stranded nucleic acid could be bound through interaction with a second strand of nucleic acid. Therefore, in opposition to argument raised at page 8 of the response, O'Neil et al., for reasons found below, does anticipate, or at least render obvious the invention of claims 35 and 8-11, which depend therefrom.

29. O'Neil et al., disclose the immobilization of "recovery primers" and "recovery tags" (nucleic acid probes and nucleic acid primers; applicants' "target receptors" and "single-stranded nucleic acids of a predetermined base sequence').

30. O'Neil et al., column 16, provides a listing of various solid supports (applicants' carrier particle) to which one or more nucleic acids are bound.

31. O'Neil, column 11, first full paragraph, teaches that different approaches to using chain terminating nucleotides can be performed, noting specifically that primers can be labeled differently, or that differently labeled chain terminating nucleotides can be added to a primer extension product.

32. O'Neil et al., column 6, teaches that in one embodiment the nucleic acid can be from 18-36 nucleotides long (primers). O'Neil et al., also discloses performing primer extension reactions, where a fluorescently labeled chain terminator is incorporated into the primer extension product. The aspect of creating a single stranded nucleic acid that is bound to a solid support (carrier) at one end and has a label at the other end (chain terminated sequencing reaction product) is considered to meet the limitation that the immobilized nucleic acids can be of considerably longer length, e.g., tens of thousands of nucleotides long.

33. O'Neil et al., are considered to meet the limitation that the nucleic aids are present in a predetermined molar ratio as they are disclosed as being used in PCR and sequencing assays, which require the usage of known concentrations of reactants.

34. In the event that O'Neil et al., do not anticipate the claimed invention, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a compound comprising nucleic acids immobilized to a carrier where the nucleic acids are of a predetermined sequence, are labeled at the end opposite to that bound to the carrier, and are present in a predetermined molar ratio as such is disclosed as being useful in conducting hybridization assays, amplification assays, and sequencing assays.

35. For the above reasons, and in the absence of convincing evidence to the contrary, claims 8-11 and 35-37 are rejected under 35 U.S.C. 102(a and e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 6,124,092 (O'Neil et al.).

Response to argument

36. At page 8 of the response applicant's representative asserts that it is not possible for O'Neil et al., to teach or render obvious the invention of claim 35 as claim 35 requires the

bonding of a single stranded nucleic acid to a carrier particle and that O'Neil teaches using double stranded nucleic acids.

37. The above argument has been fully considered and has not been found persuasive for the claim has been construed, as noted above, as encompassing both direct and indirect bonding of said single stranded nucleic acid to said carrier particle. Accordingly, the labeled single stranded is indirectly bonded to the carrier particle through its interaction with a second single stranded nucleic acid. It is further noted that applicant, through claim 36, states that the "double stranded" nucleic acid is comprised of a first and a second "single stranded nucleic acid." Given that the claims allow for indirect bonding of the first single strand, and given that said nucleic acid is present, that at least two portions of same are differently labeled and are bound to the carrier particle, the disclosure of O'Neil et al., is considered to meet the limitation of claims 35 and 8-11, which depend therefrom.

38. At page 9 of the response applicant's representative asserts:

> Please note that when the primer of O'Neill *et al.* is labeled, the first strand is bonded to the carrier and the first strand is bonded to the label. Therefore, O'Neill *et al.* do not teach or suggest the subject matter of Claim 36 when the label is on the primer.

39. The above argument has been fully considered and has not been found persuasive towards the withdrawal of the rejection. O'Neil et al., column 11, clearly teach that the primer or the primer extension product (chain terminator) can be labeled. Given that the primer extension products are used in subsequent rounds of amplification, what constitutes a "second single strand" in one round of amplification can and does serve as the "first single strand" in the subsequent round of amplification. It is noted with particularity that there is no prohibition of the first single strand from being labeled. As noted by applicant's representative, what becomes

the "first single strand" is bound to the carrier particle, as required by the claims. Given that complementary sequences will anneal/hybridize to one another, such duplex structures will be present when the carrier particles are added to the mixture (O'Neil et al., column 11).

40. Argument is advanced in that there is no predetermined ratio, and as such the rejections cannot be sustained.

41. The above argument has been fully considered and has not been found persuasive towards the withdrawal of same for O'Neil et al., column 11, clearly teach performing amplification using labeled primers, where the different primers in a multiplex reaction are labeled differently. The presence of differently labeled primers peaks directly to the establishment of a predetermined ration of labeled substances.

42. Therefore, and in the absence of convincing evidence to the contrary, the rejection is maintained.

Conclusion

43. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

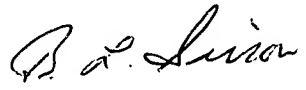
44. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

45. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

46. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

47. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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Art Unit 1634

BLS
10 January 2004